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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/532,407	04/22/2005	Adel Penhasi	030231-0158	9132

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EXAMINER	
WESTERBERG, NISSA M	
ART UNIT	PAPER NUMBER
1618	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/532,407	PENHASI ET AL.	
	Examiner	Art Unit	
	Nissa M. Westerberg	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 - 93* is/are pending in the application.

4a) Of the above claim(s) *1 - 88* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *89 - 93* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 April 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/22/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of group VI, claims 89 and 90 and the species in tables 1 through 3 in the reply filed on April 7, 2008 is acknowledged. The traversal is on the grounds that the search and examination of groups VI – VIII is not unduly burdensome.

Applicant's traversal argument in regards to groups VI – VIII is found to be persuasive. The methods of groups VII and VIII have been added to group VI, which now consists of claims 89 – 93.

As the election for the composition of the formulation of the dosage form, Applicant has elected the formulation in tables 1 – 3. These tables contain a variety of formulations. The elected claims requires a composition comprising the following elements: a) venlafaxine in the compressed tablet core, b) at least one burst controlling agent in the compressed tablet core, c) a disintegrant in the compressed tablet core, d) a water insoluble hydrophobic carrier in the outer coating and e) a water-insoluble but hydrophilic particulate matter in the outer coating. In order to further the prosecution of this Application, the Examiner has read this as an election of microcrystalline cellulose, crospovidone, ethyl cellulose and microcrystalline cellulose as components b) – e) respectively as these elements are present in the majority of formulations present in tables 1 through 3.

The requirement is still deemed proper and is therefore made FINAL.

Oath/Declaration

2. The receipt of an oath or declaration on April 25, 2005 was indicated on the Form 903 – Notice of Acceptance of Application Under 35 U.S.C. 371 and 37 CFR 1.495, mailed on October 26, 2005. However, a copy of the oath or declaration is not present in the electronic file wrapper for the instant application. The submission of a copy of this document, through the electronic submission system or by fax, is requested so that a copy of this document is present in the file wrapper.

Double Patenting

3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29

USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claims 89 – 93 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 – 7, 20 – 22, 33 and 34 of U.S. Patent No. 6,703,044 as evidenced by Lerner et al. (US 5,840,332). Although the conflicting claims are not identical, they are not patentably distinct from each other because the method claims in both applications have the same active step. The claims of the instant application and US'044 require the administration of a formulation of venlafaxine which comprises a core and an outer coating. The core comprises venlafaxine, at least one burst controlling agent and a disintegrant. The coating comprises a water insoluble hydrophobic material and a water-insoluble but hydrophilic

particulate matter. As evidenced by Lerner et al., the swelling of the hydrophilic particulate material in the outer coating upon contact with aqueous media leads to the formation of channels that lead to the delayed release of the active ingredient from the core (col 6, ln 18 – 22). As the different methods require the same composition, the composition necessarily meets the limitation of the method stated in the preamble of the claim (treating a subject and providing enhanced bioavailability in the claims of '044 and providing a therapeutic blood plasma concentration of venlafaxine over a twenty-four hour period with diminished fluctuations in blood drug concentration, providing a therapeutic blood plasma concentration of venlafaxine over a twenty-four hour period with diminished side effects and a method of obtaining improved patient compliance in venlafaxine usage in the instant application).

5. Claims 89, 91 and 93 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 42, 43, 45 and 47 – 49 of copending Application No. 10/555,310 in view of Lerner et al. (US 5,840,332). The claims of the instant application recite methods comprising the active step of administering an oral dosage form comprised of a compressed tablet core containing venlafaxine, at least one burst controlling agent and a disintegrant that is coated with a layer containing a water insoluble hydrophobic carrier and a water-insoluble but hydrophilic particulate matter.

Claims 47 – 49 of '310 recite a method for providing therapeutic blood plasma concentrations of venlafaxine over a 24 hours period comprising the active step of

administering a dosage form according to claim 1. Claims 42, 43 and 45 of '310 use the dosage form of claim 1 to provide a specific therapeutic blood plasma concentration and are being interpreted as a method of using the composition. The dosage form of claim 1 is an extended release tablet dosage form comprising a core and a coating. The core comprise venlafaxine, a filler such as microcrystalline cellulose (see claims 3 and 4; the burst control agent of the instant claims) and ethyl cellulose and a water soluble cellulosic polymer (such as hydroxypropylmethylcellulose (HPMC), see claim 6). These cellulosic polymers can function as disintegrants (see col 1, ln 7 – 10 of US 6,531,151). The coating comprises a water insoluble cellulosic polymer such as ethyl cellulose (see claim 17) and a water soluble cellulosic polymer.

'310 does not recite the inclusion of a water insoluble but hydrophilic material in the coating layer.

Lerner et al. discloses that the presence of water insoluble but hydrophilic material an outer coating layer that is insoluble and hydrophobic, such as ethyl cellulose, results in the formation of channels in the outer coating upon exposure to aqueous media. This results in the delayed release of the active ingredient from the core, which contains the active ingredient.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to add a water insoluble but hydrophilic material to the coating layer of the composition claimed in '310 because the addition of such material results in an extended release coated tablet. As the active step of the various method claims require

a composition of the same ingredients and arrangement, the limitations of the method are necessarily provided by administration of the composition.

This is a provisional obviousness-type double patenting rejection.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 89 – 93 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sherman et al. (US 6,274,171) in view of Lerner et al. (US 5,840,332).

Sherman et al. discloses a 24 hour extended release dosage form of venlafaxine hydrochloride (abstract). The extended release dosage form provides a method for providing a single dose, therapeutic blood plasma serum level over a 24-hour period (col 2, ln 16 – 19). Administration of the same dosage form also provides a flattened drug plasma concentration over time (col 2, ln 20 – 22) and reduces levels of nausea and the incidence of emesis (col 2, ln 46 - 49), common side effects of the administration of plural daily doses of venlafaxine (col 2, ln 7 – 11). The extended release formulations comprise spheroids of venlafaxine hydrochloride, microcrystalline cellulose, exemplified by Applicant as a burst control agent and optionally, hydroxypropylmethyl cellulose (HPMC; col 2, ln 63 – col 3, ln 1). Applicant does not provide an exclusive list of compounds that can act as disintegrants (preferable compounds are exemplified on p 8 of the instant specification), but HPMC can function as a disintegrant (evidenced by US 6,531,151 in which HPMC is exemplified as a compound that can act as a disintegrant; col 1, ln 7 – 10). These spheroids are coated with a mixture of ethyl cellulose, exemplified by Applicant as a water insoluble hydrophobic carrier, and HPMC (col 3, ln 1 – 2). While not explicitly exemplified,

spheroid formulations in which the core also comprises the binder polyvinylpyrrolidone (povidone) were also prepared (col 5, ln 1 – 8).

Sherman et al. does not disclose a delayed burst release formulation as required by the instant application in which the outer coating comprises both a water insoluble hydrophobic carrier and water-insoluble but hydrophilic particulate matter. A delayed burst release after at least 3 hours is also not disclosed.

Lerner et al. discloses a delivery device for targeted delivery of active ingredients which comprise a core, comprising a drug in combination with a carrier material, and a coating (col 6, ln 2 – 5). The core of the dosage form can take the form of a compressed tablet (col 6, ln 9 – 10). The coating comprises a material that is not soluble in water within which hydrophilic, non-water-soluble particles are embedded (the water insoluble hydrophobic carrier and water-insoluble but hydrophilic particulate matter of the instant claims; col 6, ln 16 – 18). The introduction of water or aqueous fluids causes the particulate matter to swell, which eventually leads to the formation of channels from the outer part of the device to the drug containing core, allowing for release of the active ingredient from the core (col 6, ln 18 – 22). The location of the drug release is determined by such parameters as the thickness of the outer coating, the amount and type of particulate matter embedded in the coating, the particle size distribution of the particulate matter and the core carrier material (col 6, ln 31 – 36). The drug delivery system can delivery drugs to the colon (col 6, ln 42 – 43). Suitable materials for the core include, but are not limited to, combinations of pectin, calcium pectinate, HPMC, lactose, starch, polyvinylpyrrolidone (povidone), microcrystalline cellulose and normal

pharmaceutical additives and excipients (col 8, ln 47 – 54). The particulate material used in the outer core includes polysaccharides such as calcium pectinate, calcium alginate, insoluble starch, microcrystalline starch, cellulose and microcrystalline cellulose (col 9, ln 7 – 14). Examples of water-insoluble carrier materials include various EUDRAGIT® polymers and ethylcellulose (col 9, ln 44 – 45, 62 – 65). In one embodiment, the ingredients used and the size of the particulates and thickness of the coating layer allow for the delivery of a soluble drug to the colon since it affords an approximately four hour delay in drug release under *in vitro* conditions (col 11, ln 56 – col 12, ln 2).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to prepare a delayed drug delivery device, as taught by Lerner et al., using the drug venlafaxine given the improved blood plasma levels and side effects of extended release dosage formulations taught by Sherman et al. Sherman et al. discloses that the administration of extended release dosage forms of venlafaxine flattens the blood concentration of the active ingredient and decreases the side effects of nausea and vomiting frequently associated with venlafaxine administration. Lerner et al. discloses that a compressed tablet coated with a layer comprised of a water insoluble hydrophobic carrier and a water-insoluble but hydrophilic particulate material is one extended release formulation that provide a delayed burst release of active ingredient to the colon. Neither reference teaches that such extended release dosage forms of venlafaxine improves patient compliance, as recited in claim 93. However, the active step of the method requires the administration of the dosage form taught by

Sherman et al. and Lerner et al. and therefore the limitations of this claims are necessarily met by the cited prior art.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nissa M. Westerberg whose telephone number is (571)270-3532. The examiner can normally be reached on M - F, 8 a.m. - 4 p.m. ET. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

NMW